AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for screening a combination of treatments to specifically target a disease process that impacts gene expression, said method comprising the steps of:

(a) providing differential expression levels of diseased tissue samples relative to at least one reference tissue for respective features of microarrays used to calculate the differential expression levels;

(b) for respective features of respective microarrays for each diseased tissue sample, providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples;

(f) repeating steps (c) – (e) with a different treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments;

(g) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together; and

(h) selecting treatments by identifying the treatment-response phenotypic signatures caused by those treatments, and which are clustered with phenotypic signatures representing differential expression levels representative of the diseased tissue samples.

2. (Original) The method of claim 1, wherein said providing differential expression levels further comprises processing the diseased tissue samples and the at least one reference tissue using microarray technology to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

3. (Original) The method of claim 1, wherein said providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively,

comprises generating the phenotypic/genotypic signatures based on the differential expression levels provided.

4. (Original) The method of claim 1, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

5. (Currently Amended) The method of claim 1, further comprising the steps of:

labeling the phenotypic/genotypic ~~phenotypic~~ signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (g) and (h).

6. (Original) The method of claim 1, wherein said clustering operation includes finding a density center of a cluster, and calculating distances of the phenotypic signatures, belonging to the cluster, from the density center.

7. (Original) The method of claim 6, wherein the selection of treatments is made to address a broad spectrum of genes involved in the disease process of the diseased tissues.

8. (Original) The method of claim 7, wherein the treatments are selected by selecting treatment-response signatures within a cluster and having varying distances from the density center.

9. (Original) The method of claim 1, wherein said phenotypic signatures are normalized prior to said clustering.

10. (Original) The method of claim 5, wherein said phenotypic signatures are normalized prior to said clustering.

11. (Original) A method comprising forwarding a result obtained from the method of claim 1 to a remote location.

12. (Original) A method comprising transmitting data representing a result obtained from the method of claim 1 to a remote location.

13. (Original) A method comprising receiving a result obtained from a method of claim 1 from a remote location.

14. (Original) The method of claim 2, wherein said processing to obtain differential expression levels comprises processing a diseased-tissue sample and the reference tissue on a two-color, two channel microarray apparatus.

15. (Original) The method of claim 2, wherein said processing to obtain differential expression levels comprises processing a diseased-tissue sample on a single channel microarray apparatus, processing the reference tissue on a single channel microarray apparatus, and comparing the results of the processing.

16. (Original) The method of claim 1, wherein each treatment-response value comprises a concentration level or amount of the treatment used to block or retard the growth of the tissue by a predetermined percentage over a predetermined period of time after treatment.

17. (Original) The method of claim 1, wherein each treatment-response value comprises a value characterizing the amount of blocking or retardation of growth of the tissue over a predetermined period of time after treatment with a fixed amount of the treatment.

18. (Original) The method of claim 1, further comprising generating at least one phenotypic signature representing treatment-response values of each of the diseased tissue samples resultant from treating the diseased tissue samples with at least one treatment having known undesirable characteristics for treatment of the diseased tissues;

including that at least one phenotypic signature resulting from said treatment having known undesirable characteristics with all other signatures included in performing the clustering step (g); and

discarding any phenotypic signature representing treatment-response values from candidacy for the selection step (h) when the phenotypic signature is less than or equal to a predefined distance from a location of the at least one phenotypic signature resulting from treatment with a treatment having known undesirable characteristics.

19. (Original) The method of claim 18, wherein said known undesirable characteristics comprise an unacceptable level of toxicity.

20. (Original) The method of claim 18, wherein said known undesirable characteristics comprise an insufficient efficacy.

21. (Original) A method of augmenting an original or existing single treatment or treatment combination for a disease with at least one additional treatment that covers gene activity of the disease not addressed by the original or existing treatment, said method comprising the steps of:

(a) providing differential expression levels of diseased tissue samples relative to at least one reference tissue for respective features of microarrays used to calculate the differential expression levels;

(b) for respective features of respective microarrays for each diseased tissue sample, providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively;

(c) treating the diseased tissue samples with the original or existing single treatment or combination treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples as effected by the original or existing single or combination treatment;

(f) treating the diseased tissue samples with a treatment that is not included in the original or existing single or combination treatment;

(g) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(h) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples as effected by the treatment that is not included in the original or existing single or combination treatment;

(i) repeating steps (f) – (h) with a different treatment that is also not included in the original or existing single or combination treatment at least once so that multiple phenotypic signatures have been generated for multiple treatments not included in the original or existing single or combination treatment;

(j) performing a clustering operation based on the phenotypic/genotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together; and

(k) selecting at least one treatment by identifying the treatment-response phenotypic signatures caused by the at least one treatment, and which are clustered with phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, as well as with phenotypic signatures representing differential expression levels representative of the diseased tissue samples, but separated from the phenotypic signatures identifying the treatment-response phenotypic signatures caused by the treatment or treatments in the original treatment, so as to address disease-gene activity not currently addressed by the treatment or treatments in the original or existing treatment.

22. (Original) The method of claim 21, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

23. (Currently Amended) The method of claim 21, further comprising the steps of:

labeling the phenotypic/genotypic ~~phenotypic~~ signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (j) and (k).

24. (Withdrawn) A system for screening a combination of treatments to specifically target a disease process, said system comprising:

means for generating a phenotypic signature representing differential expression levels of each of a plurality of diseased tissue samples relative to at least one reference tissue for respective features of

microarrays used to calculate differential expression levels of the diseased tissue samples and the at least one reference tissue;

means for measuring a treatment-response value with respect to each the diseased tissue samples after treating each diseased tissue sample with a treatment;

means for generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples; and

means for performing a clustering operation while considering the phenotypic signatures of the differential expression levels and the phenotypic signature of the compound-response values together.

25. (Withdrawn) The system of claim 24, further comprising microarray apparatus for processing the diseased tissue samples and the at least one reference tissue to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

26. (Withdrawn) The system of claim 24, wherein multiple treatments are successively and independently applied to treat the diseased tissues, with respective treatment-response values measured for each and a treatment-response phenotypic signature is generated for each treatment applied.

27. (Withdrawn) The system of claim 24, further comprising means for generating "out of phase" differential expression phenotypic signatures by inverting said phenotypic signatures representing the differential expression levels.

28. (Withdrawn) The system of claim 27, wherein said means for clustering includes said "out of phase" differential expression phenotypic signatures with said phenotypic signatures representing the differential expression levels and said phenotypic signatures of the treatment-response values when performing said clustering operation.

29. (Withdrawn) The system of claim 24, further comprising means for determining a center of density of a cluster identified by said means for clustering, and means for determining a distance of a phenotypic signature found to belong to said cluster, from said center of density.

30. (Original) A method for determining phase relationships between treatment responses of diseased tissues to treatments which are applied thereto and expression profiles of the diseased tissues, said method comprising the steps of:

(a) providing differential expression levels of the diseased tissue samples relative to at least one reference tissue for respective features of microarrays used to calculate the differential expression levels;

(b) for respective features on respective microarrays for each disease tissue sample, providing a phenotypic signature representing the differential expression level for each tissue sample for that feature, respectively;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples;

(f) comparing the treatment-response phenotypic signature with the differential expression level phenotypic signatures for similarity; and

(g) targeting gene profiles effected by the treatment based upon the similarity results.

31. (Original) The method of claim 30, wherein said providing differential expression levels further comprises processing the diseased tissue samples and the at least one reference tissue using microarray technology to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

32. (Original) The method of claim 30, wherein said providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively, comprises generating the phenotypic/genotypic signatures based on the differential expression levels provided.

33. (Original) The method of claim 30, wherein each said treatment is selected from the group consisting of: a drug, a combination of drugs, a compound, a combination of compounds, radiation, a genetic sequence, a combination of genetic sequences, heat, cryogenics and a combination of two or more of any of the previous members in this group.

34. (Currently Amended) The method of claim 30, further comprising the steps of:

labeling the phenotypic/genotypic ~~phenotypic~~ signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (f) and (g).

35. (Withdrawn) A combination of compounds for treating cancer, said combination comprising at least two compounds selected from the group consisting of: Sevinon, or a family member thereof; Paclitaxel-Taxol; Gemcitabine and Mitoxantrone.

36. (Withdrawn) The combination of claim 35, wherein said combination comprises a compound from each of Sevinon, or a family member thereof; Paclitaxel-Taxol; Gemcitabine and Mitoxantrone.

37. (Withdrawn) The combination of claim 35, for treatment of lung cancer.

38. (Withdrawn) A computer readable medium carrying one or more sequences of instructions for screening a combination of treatments to specifically target a disease process, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the steps of:

(a) providing differential expression levels of diseased tissue samples relative to at least one reference tissue for respective features of microarrays used to calculate the differential expression levels;

(b) for respective features of respective microarrays for each diseased tissue sample, providing a phenotypic signature representing the differential expression level for each tissue sample for that feature, respectively;

(c) treating the diseased tissue samples with a treatment;

(d) measuring a treatment-response value with respect to each of the diseased tissue samples as effected by the treatment;

(e) generating a phenotypic signature representing the treatment-response values of each of the diseased tissue samples;

(f) repeating steps (c) – (e) with a different treatment at least once so that multiple phenotypic signatures has been generated for multiple treatments;

(g) performing a clustering operation based on the phenotypic signatures of the differential expression levels and the phenotypic signatures of the treatment-response values together; and

(h) selecting at least one treatment by identifying the treatment-response phenotypic signatures caused by those treatments, and which are clustered with phenotypic signatures representing differential expression levels representative of the diseased tissue samples.

39. (Withdrawn) The computer readable medium of claim 38, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the further step of:

processing the diseased tissue samples and the at least one reference tissue using microarray technology to obtain the differential expression levels of the diseased tissues relative to the at least one reference tissue.

40. (Withdrawn) The computer readable medium of claim 38, wherein said providing a phenotypic/genotypic signature representing the differential expression level for each tissue sample for that feature, respectively, comprises generating the phenotypic/genotypic signatures based on the differential expression levels provided.

41. (Withdrawn) The computer readable medium of claim 38, wherein execution of one or more sequences of instructions by one or more processors causes the one or more processors to perform the further steps of:

labeling the phenotypic signatures representing the differential expression levels as "in phase" signatures;

generating "out of phase" signatures by inverting the "in phase" signatures; and

including the "out of phase" signatures with the "in phase" signatures and the treatment-response signatures when performing steps (g) and (h).